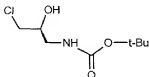


120.83, 124.67, 127.65, 138.06 and 155.40 ; MS (EI), m/z (relative intensity) 222 (37) and 164 (100).

**EXAMPLE 3**

5



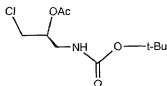
- 10 **Preparation of tert-butyl (2S)-3-chloro-2-hydroxypropylcarbamate, alternatively named N-((2S)-3-chloro-2-hydroxypropyl)(tert-butoxy)carboxamide (Compound IV, R<sup>3</sup> =t-butyl, X=Cl)**

- 15 To a slurry of (2S) 1-amino-3-chloro-2-propanol hydrochloride, (750.3 g, 5138 mmol) in methylene chloride (2728 g) and methanol (435.4 g) at -13°C was added a solution of di-tert-butyl dicarbonate (1178.3 g, 5399 mmol, 1.05 eq) in methylene chloride (1144 g) followed by triethylamine (572.3 g, 5656 mmol, 1.10 eq). The resultant 13°C slurry was then warmed and stirred at 17-19°C for 1 h. The resultant solution was concentrated under reduced pressure to a 2182 g slurry. Toluene (959.3 g) and water (975.5 g) were added and the phases separated. The
- 20 organic phase was washed with water (500 ml) and the aqueous serial back extracted with toluene (2 X 500 ml). The combined organics were concentrated under reduced pressure to 1592 g. Isooctane (5853 g) was added and the mixture seeded and stirred at 20-25°C for 17 h. The precipitated product was collected by vacuum filtration, washed with isooctane (400 g) and dried in a nitrogen stream to afford Compound IV,
- 25 wherein R<sup>3</sup> =t-butyl, X=Cl, (1024 g, 95.1 %): GC retention time = 8.2 min (15 meter DB5 capillary column, 70°C for 2 min, then ramp 10°C/min); <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 400 MHz) δ: 5.08 (bs, 1H), 3.92 (m, 2H), 3.57 (bs, 1H), 3.55 (m, 1H), 3.42 (m, 1H), 3.24

(m, 1H), 1.45 (s, 9H);  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  28.35 (q), 43.90 (t), 46.52 (t), 71.23 (d), 80.13 (s), 157.24 (s).

#### EXAMPLE 4

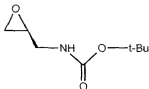
5



- 10 **Preparation of (1S)-2-[(tert-butoxycarbonyl)amino]-1-(chloromethyl)ethyl acetate, alternatively named N-((2S)-3-chloro-2-acetoxypropyl)(tert-butoxy)carboxamide (Compound V,  $\text{R}^3$ =t-butyl,  $\text{R}^4$ =Ac, X=Cl)**

- To a solution of tert-butyl (2S)-3-chloro-2-hydroxypropylcarbamate  
15 (0.9928 g, 4.74 mmol) in THF (7 ml) and triethylamine (0.7303 g, 7.22 mmol, 1.52 eq) was added acetic anhydride (0.6033 g, 5.91 mmol, 1.25 eq) and N, N-dimethyl-4-aminopyridine (0.00265 g, 0.0217 mmol, 0.0046 eq). The solution was stirred at room temperature for 3 days. Toluene (10 g) and saturated aqueous sodium bicarbonate (10 ml) was added and the phases separated. The aqueous was washed  
20 with a mixture of toluene (10 ml) and THF (5 ml) and the combined organics dried on magnesium sulfate. The organics were concentrated under reduced pressure to 1.6 g and heptane (7.3 g) added. After standing for 25 days at 20-25 °C, a precipitate formed. Heptane (10.8 g) was added and the precipitate collected by vacuum filtration, washed with heptane (10 ml) and dried in a nitrogen stream to give  
25 Compound V, wherein  $\text{R}^3$ =t-butyl,  $\text{R}^4$ =Ac, X=Cl, 0.3803 g (31.9%):  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 1.45 (s, 9 H), 2.11 (s, 3 H), 3.41 (m, 2 H), 3.67 (m, 2 H), 4.79 (s, 1 H), 5.07 (t,  $J$  = 5.2 Hz, 1 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) 20.92 (q), 28.33 (q), 41.43 (t), 43.30 (t), 72.16 (d), 79.89 (s), 155.85 (s), 170.26 (s); MS (EI) for  $\text{C}_{10}\text{H}_{18}\text{ClNO}_4$   $m/z$  251  $\text{M}^+$ ;  $[\alpha]^{22}_{\text{D}}$  (-2,  $\text{C}$  = 1.0, methylene chloride); Anal. Calcd for  $\text{C}_{10}\text{H}_{18}\text{ClNO}_4$ : C, 47.72; H, 7.21; N, 5.57. Found: C, 47.70; H, 7.17; N, 5.55.  
30

**EXAMPLE 5**



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**Preparation of tert-butyl (2S)oxiranylmethylcarbamate, alternatively named N-(((2S)oxiran-2-yl)methyl)(tert-butoxy)carboxamide (Compound II, R<sup>3</sup> =t-butyl, X=Cl)**

- 10 To a solution of tert-butyl (2S)-3-chloro-2-hydroxypropylcarbamate (19.98 g, 95.29 mmol) in methanol (50.0 ml) at 13 °C was added lithium t-butoxide (8.40 g, 104.9 mmol, 1.10 eq) while maintaining less than 22 °C. The mixture was stirred at 8 to 20 °C for 15 min and water (200 ml) followed by methylene chloride (200 ml) was added. The phases were separated and the aqueous washed with
- 15 methylene chloride (135 ml). The combined organics were dried on magnesium sulfate and concentrated to an oil. Column chromatography on silica gel (0 to 4% methanol in methylene chloride eluent) gave Compound II, wherein R<sup>3</sup> =t-butyl, X=Cl, as a white solid (14.26 g, 86.4%): m.p. 45-49 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 1.448 (s, 9 H), 2.59 (s, 1 H), 2.78 (t, J = 4 Hz, 1 H), 3.09 (s, 1 H), 3.20 (dt, J = 14, 6
- 20 Hz, 1 H), 3.53 (d, J = 15 Hz, 1 H), 4.85 (s, 1 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) 28.28 (q), 41.72 (t), 45.04 (t), 50.85 (d), 79.61 (s), 155.96 (s); MS (CI<sup>+</sup>) for C<sub>8</sub>H<sub>15</sub>NO<sub>3</sub> m/z 174 (M+H)<sup>+</sup>; [α]<sub>D</sub><sup>22</sup> (-13, C + 1.0, methylene chloride); Anal. Calcd for C<sub>8</sub>H<sub>15</sub>NO<sub>3</sub>: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.17; H, 8.54; N, 8.00.